January 29, 2004

Dr. Mark A. Thomson
Manager, Toxicology & International Product Registration
Crompton Corporation
199 Benson Road
Middlebury, CT 06749

Dear Dr. Thomson:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Dimethyl 3,3'-thiobispropionate posted on the ChemRTK HPV Challenge Program Web site on September 30, 2003. I commend Crompton Corporation for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Crompton advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Dimethyl 3,3'-Thiobispropionate

Summary of EPA Comments

The sponsor, Crompton Corporation, submitted a test plan and robust summaries to EPA for dimethyl 3,3'-thiobispropionate (CAS No.4131-74-2), dated September 3, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on September 30, 2003.

EPA has reviewed this submission and reached the following conclusions:

1. Analogue Justification. EPA agrees that data on the structural analogue didodecyl 3,3'-thiodipropionate can be used to address the SIDS endpoints for dimethyl 3,3'-thiobispropionate because both esters are hydrolyzed to a common metabolite, thiodipropionic acid (TDPA)

2. Physicochemical Properties. The data provided for melting point and partition coefficient are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured boiling point, vapor pressure, and water solubility data. For the boiling point, however, testing is not required because EPA found measured values in the literature; these values need to be incorporated in the test plan and robust summary.

3. Environmental Fate. The data provided for photodegradation and stability in water are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured ready biodegradation data and recalculate the fugacity model estimates using measured data.

4. Health Effects. The submitted data for acute, repeated-dose, reproductive, and developmental toxicity are adequate for the purposes of the HPV Challenge Program. The submitter needs to address deficiencies in the robust summaries. Although the submitter has proposed conducting Ames and in vitro chromosomal assays, EPA believes that adequate data are available for the genetic toxicity endpoints in the revised submission of the thiodipropionates category.

5. Ecological Effects. The ecological data are not adequate for the purposes of the HPV Challenge Program because the submitter only provided estimated values using ECOSAR.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the Dimethyl 3,3'-thiobispropionate Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility).

Boiling point. The submitter estimated a value of 242°C using the program MPBPWIN v1.4. According to OECD TG 103, boiling point values need to be measured if the calculated/estimated value is not >300°C. However, EPA found seven measured boiling points of dimethyl 3,3'-thiobispropionate at reduced pressures in the literature (see below). These values were converted to values at normal pressure (760 mmHg), and they range from approximately 260°-300 °C using the NOMO5 program. They indicate that the substance might decompose when it is heated above boiling at normal pressure. The submitter needs to replace the estimated value with the measured values at reduced pressures in the test plan and robust summary.

Boiling Point (literature)	148°C at 18 mmHg[a] 161-162°C at 18 mmHg[b] 162-164°C at 18 mmHg[b, d] 158-159°C at 10 mmHg[b] 148.5-149°C at 8 mmHg[b] 138-139°C at 6 mmHg[b,d] 130°C at 2 mmHg[c]

[a]Lide DR (ed). 2000. CRC Handbook of Chemistry and Physics, 81st Edition, New York, NY: CRC Press, p. 3-282.
[b]Beilstein Online database; searched December 4, 2003.
[c]Kirk-Othmer Encyclopedia of Chemical Technology. 1997. 4th ed. Volumes 1 to present. New York, NY: John Wiley and Sons. Labat, Y; Thioglycolic Acid. v. 24, p. 7.
[d]The preparation of Methyl b-thiodipropionate, Organic Syntheses, CV4, 669.
http://www.orgsyn.org/orgsyn/orgsyn/prepContent.asp?rxntypeid=11&prep=CV4P0669 (12/23/2003)

Vapor pressure. The submitter estimated a value of 0.055 hPa (0.041 mmHg) at 25 °C using the program MPBPWIN v1.40. According to OECD TG 104, vapor pressure values need to be measured if the estimated value is >$1x10^{-5}$ Pa ($7.5x10^{-8}$ mmHg). The submitter needs to provide measured vapor pressure data for this chemical.

Water solubility. The submitter provided neither measured nor estimated water solubility data. The submitter stated that this substance is practically insoluble in water based on a Material Safety Data Sheet (Crompton Corporation, 2002). EPA estimated a water solubility of 5,900 mg/L at 25 °C using the program WSKOWWIN v1.41. According to OECD TG 105, water solubility values need to be measured if the estimated value is >1 µg/L. The submitter needs to provide measured water solubility data.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

Biodegradation. The submitter provided estimated data using the program BIOWIN v.4.00. However, in order to meet the guidelines of the HPV Challenge Program, the submitter needs to provide measured ready biodegradation data following OECD TG 301.

Fugacity. The submitter needs to recalculate the fugacity model estimates using measured data. The use of estimated values introduces uncertainties that then become magnified in modeling applications.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Analogue Justification. The submitter has provided health effects data for didodecyl 3,3'-thiodipropionate to address the health effects endpoints for dimethyl 3,3'-thiobispropionate. Both compounds are esters of TDPA. The submitter has provided toxicokinetics data showing that these esters are completely absorbed and hydrolyzed to a common metabolite, TDPA, which is further hydrolyzed and rapidly eliminated in the urine. The toxicity of both esters will essentially be the toxicity of TDPA. EPA agrees with this approach.

The submitted data for acute, repeated-dose, reproductive, and developmental toxicity are adequate. However, the submitter needs to address deficiencies in the robust summaries. In addition, although the submitter has proposed conducting Ames and in vitro chromosomal assays, EPA believes that adequate data are available for genetic toxicity endpoints in the revised submission of the thiodipropionates category. Therefore, no further testing is necessary.

Ecological Effects (fish, invertebrates, and algae).

For all ecological endpoints, the submitter provided only estimated data using ECOSAR. In order to meet the guidelines of the HPV Challenge Program, the submitter needs to provide either measured data on the subject chemical or predicted SAR values plus measured data on an analogue.

The submitter claims that no further ecotoxicity testing is necessary because of the chemical's low water solubility and high estimated log Kow value. However, a quantitative water solubility value was not provided, and the estimated log Kow value of 0.98 is not considered high enough to rule out the need for ecotoxicity testing.

Specific Comments on the Robust Summaries

Health Effects

Acute Toxicity. The submitter needs to clarify the discrepancy between the study type (LD_{50})and the reference (6) for the second acute oral toxicity study summary. The reference indicates that it is a mutagenicity study.

Repeated-Dose Toxicity. The submitter needs to indicate the statistical significance of the affected clinical chemistry parameters and to list the organs/tissues that were weighed and evaluated histopathologically.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.